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(22) Date of filing: **25.11.1987**

(54) **Use of hydroxycarboxylic acids and derivatives for the preparation of topical dermatologic compositions for the treatment of wrinkles**

Verwendung von Hydroxycarbonsäuren und Derivaten zur Herstellung topischer dermatologischer Zubereitungen zur Behandlung von Falten

Utilisation d'acides hydroxycarboxyliques et leurs dérivés pour la préparation de compositions dermatologiques topiques pour le traitement de rides

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(56) References cited:
EP-A- 0 007 785 **EP-A- 0 086 070**
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Remarks:

The file contains technical information submitted
after the application was filed and not included in
this specification

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Description

This invention relates generally to the treatment of wrinkles using compositions containing hydroxycarboxylic acids or related compounds.

As will be subsequently described in detail, we initially discovered that alpha hydroxy or keto acids and their derivatives were effective in the topical treatment of disease conditions such as dry skin, ichthyosis, eczema, palmar and plantar hyperkeratoses, dandruff, acne and warts.

We have further discovered that hydroxyacids or related compounds wherein incorporated into a therapeutic composition can substantially enhance topical effects of cosmetic and pharmaceutical agents. See also parent application No. 87 117 405.8.

In our prior U.S. Patent No. 3,879,537 entitled "Treatment of Ichthyosiform Dermatoses" we described and claimed the use of certain alpha hydroxy acids, alpha keto acids and related compounds for topical treatment of fish-scale like ichthyotic conditions in humans. In our U.S. Patent No. 3,920,835 entitled "Treatment of Disturbed Keratinization" we described and claimed the use of these certain alpha hydroxy acids, alpha keto acids and their derivatives for topical treatment of dandruff, acne, and palmar and plantar hyperkeratosis.

In our prior U.S. Patent No. 4,105,783 entitled "Treatment of Dry Skin" we described and claimed the use of alpha hydroxy acids, alpha keto acids and their derivatives for topical treatment of dry skin. In our recent U.S. Patent No. 4,246,261 entitled "Additives Enhancing Topical Corticosteroid Action" we described and claimed that alpha hydroxy acids, alpha keto acids and their derivatives, in small amounts could greatly enhance the therapeutic efficacy of corticosteroids in topical treatment of psoriasis, eczema, seborrheic dermatitis and other inflammatory skin conditions.

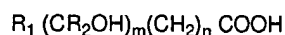
In our more recent U.S. Patent No. 4,363,815 entitled "Alpha Hydroxy acids, Alpha Keto acids and Their Use in Treating Skin Conditions" we described and claimed that alpha hydroxy acids and alpha keto acids related to or originating from amino acids, whether or not found in proteins, were effective in topical treatment of skin disorders associated with disturbed keratinization or inflammation. These skin disorders include dry skin, ichthyosis, palmar and plantar hyperkeratosis, dandruff, Darier's disease, lichen simplex chronicus, keratoses, acne, psoriasis, eczema, pruritus and possibly warts and herpes.

In our most recent U.S. Patent No. 4,518,789 entitled "Phenyl Alpha-Acyloxyacetamide Derivatives and Their Therapeutic Use" we described and claimed that phenyl alpha acyloxyacetamide derivatives in topical or systemic administration were useful and effective for pruritus, atopic dermatitis, eczema, psoriasis, acne, dry skin, dandruff, malodors of integumental areas, various aches, pains and discomforts of skin, joints and other body parts in humans and domestic animals.

EP 007785 describes cosmetically acceptable skin treatment compositions comprising a skin benefit inducing amount of an hydroxylated carboxylic acid having from 4 to 12 carbon atoms in the molecule which reduce the dryness or flakiness of skin and which can improve the suppleness or smoothness of skin.

EP 086070 describes a composition for treating an epidermal-related skin disorder (acne) by increasing the extensibility of the stratum corneum or increasing the skin plasticisation.

The enhancing compounds of the instant invention are hydroxycarboxylic acids and related compounds. There are three groups of such hydroxyacids. The first is hydroxymonocarboxylic acids having the following chemical structure:



wherein

$R_1, R_2 = H$, alkyl, aralkyl or aryl group of saturated or unsaturated, straight or branched chain or cyclic form, having 1 to 25 carbon atoms.

$m = 1, 2, 3, 4, 5, 6, 7, 8$ or 9

$n = 0$ or a numerical number up to 23

When $n = 0$ and $m = 1$ or more, the hydroxymonocarboxylic acid is also called aldonic acid. The name comes from a carbohydrate, aldose, which may be oxidized to aldonic acid by the oxidation of the aldehyde group in aldose to the carboxylic group.

The hydroxymonocarboxylic acid may be present as a free acid, lactone, or salt form. The lactone form could be either inter or intramolecular lactone, however, most common ones are intramolecular lactones with a ring structure formed by elimination of one or more water molecules between a hydroxy group and the carboxylic group. Since the hydroxymonocarboxylic acids are organic in nature, they may form a salt or a complex with an inorganic or organic base such as ammonium hydroxide, sodium or potassium hydroxide, or triethanolamine.

The hydroxymonocarboxylic acid and its related compounds may also exist as stereoisomers such as D, L, and DL forms.

The typical alkyl, aralkyl and aryl groups for R_1 and R_2 include methyl, ethyl, propyl, isopropyl, benzyl and phenyl.

The hydrogen atoms of the R_1 and R_2 and $(CH_2)_n$ may be substituted by a nonfunctional element such as F, Cl, Br, I, S or a radical such as a lower alkyl or alkoxy, saturated or unsaturated, having 1 to 9 carbon atoms. Representative hydroxymonocarboxylic acids are listed below:

- 5 1. 2-Hydroxyacetic acid (Glycolic acid)
 $R_1=H, R_2=H, m=1, n=0$
2. 2-Hydroxypropanoic acid (Lactic acid)
 $R_1=CH_3, R_2=H, m=1, n=0$
3. 2-Methyl 2-hydroxypropanoic acid (Methylactic acid)
 $R_1=CH_3, R_2=CH_3, m=1, n=0$
- 10 4. 2-Hydroxybutanoic acid
 $R_1=C_2H_5, R_2=H, m=1, n=0$
5. Phenyl 2-hydroxyacetic acid (Mandelic acid)
 $R_1=C_6H_5, R_2=H, m=1, n=0$
- 15 6. Phenyl 2-methyl 2-hydroxyacetic acid (Atrolactic acid)
 $R_1=C_6H_5, R_2=CH_3, m=1, n=0$
7. 3-Phenyl 2-hydroxypropanoic acid (Phenyllactic acid)
 $R_1=C_6H_5, R_2=H, m=1, n=1$
8. 2,3-Dihydroxypropanoic acid (Glyceric acid)
 $R_1=H, R_2=H, m=2, n=0$
- 20 9. 2, 3, 4-Trihydroxybutanoic acid
 $R_1=H, R_2=H, m=3, n=0$
10. 2, 3, 4, 5-Tetrahydroxypentanoic acid
 $R_1=H, R_2=H, m=4, n=0$
- 25 11. 2, 3, 4, 5, 6-Pentahydroxyhexanoic acid
 $R_1=H, R_2=H, m=5, n=0$
12. 2-Hydroxydodecanoic acid (alpha hydroxylauric acid)
 $R_1=C_{10}H_{21}, R_2=H, m=1, n=0$
13. 2, 3, 4, 5, 6, 7-Hexahydroxyheptanoic acid
 $R_1=H, R_2=H, m=6, n=0$
- 30 14. Diphenyl 2-hydroxyacetic acid (benzilic acid)
 $R_1=C_6H_5, R_2=C_6H_5, m=1, n=0$
15. 4-Hydroxymandelic acid
 $R_1=C_6H_4(OH), R_2=H, m=1, n=0$
- 35 16. 4-Chloromandelic acid
 $R_1=C_6H_4(Cl), R_2=H, m=1, n=0$
17. 3-Hydroxybutanoic acid
 $R_1=CH_3, R_2=H, m=1, n=1$
18. 4-Hydroxybutanoic acid
 $R_1=H, R_2=H, m=a, n=2$
- 40 19. 2-Hydroxyhexanoic acid
 $R_1=C_4H_9, R_2=H, m=1, n=0$
20. 5-Hydroxydodecanoic acid
 $R_1=C_7H_{15}, R_2=H, m=1, n=3$
- 45 21. 12-Hydroxydodecanoic acid
 $R_1=H, R_2=H, m=1, n=10$
22. 10-Hydroxydecanoic acid
 $R_1=H, R_2=H, m=1, n=8$
23. 16-Hydroxyhexadecanoic acid
 $R_1=H, R_2=H, m=1, n=14$
- 50 24. 2-Hydroxy-3-methylbutanoic acid
 $R_1=C_3H_7, R_2=H, m=1, n=0$
25. 2-Hydroxy-4-methylpentanoic acid
 $R_1=C_4H_9, R_2=H, m=1, n=0$
- 55 26. 3-Hydroxy-4-methoxymandelic acid
 $R_1=C_6H_3(OH)(OCH_3), R_2=H, m=1, n=0$
27. 4-Hydroxy-3-methoxymandelic acid
 $R_1=C_6H_3(OH)(OCH_3), R_2=H, m=1, n=0$
28. 2-Hydroxy-2-methylbutanoic acid

$R_1 = C_2H_5$, $R_2 = CH_3$, $m=1$, $n=0$

29. 3-(2-Hydroxyphenyl) lactic acid

$R_1 = C_6H_4(OH)CH_2$, $R_2 = H$, $m=1$, $n=0$

30. 3-(4-Hydroxyphenyl) lactic acid

$R_1 = C_6H_4(OH)CH_2$, $R_2 = H$, $m=1$, $n=0$

31. Hexahydromandelic acid

$R_1 = C_6H_{11}$, $R_2 = H$, $m=1$, $n=0$

32. 3-Hydroxy-3-methylpentanoic acid

$R_1 = C_2H_5$, $R_2 = CH_3$, $m=1$, $n=1$

33. 4-Hydroxydecanoic acid

$R_1 = C_6H_{13}$, $R_2 = H$, $m=1$, $n=2$

34. 5-Hydroxydecanoic acid

$R_1 = C_5H_{11}$, $R_2 = H$, $m=1$, $n=3$

35. Aleuritic acid

$R_1 = C_6H_{12}(OH)$, $R_2 = H$, $m=2$, $n=7$

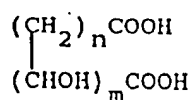
The linear lactic acid polymer is an intermolecular lactone formed by elimination of one water molecule between the hydroxy group of one molecule of lactic acid and the carboxylic group of a second molecule of lactic acid. The common linear lactic acid polymer may contain 3 lactic acid units.

Ribonic acid is one of the stereoisomers of 2, 3, 4, 5-tetrahydroxy-pentanoic acid, and the corresponding lactone is ribonolactone. Gluconic acid, galactonic acid, gulonic acid and mannonic acid are typical 2, 3, 4, 5, 6-pentahydroxyhexanoic acids and their corresponding lactones are gluconolactone, galactonolactone, gulonolactone and mannonolactone respectively. The related compounds of hydroxymonocarboxylic acids are ketomonocarboxylic acids which are formed from the former by an oxidation reaction or in vivo by a dehydrogenase enzyme. For example, 2-ketopropanoic acid (pyruvic acid) and 2-hydroxypropanoic acid (lactic acid) are converted to each other in vivo by the enzyme, lactate dehydrogenase. Although pure pyruvic acid (liquid form) can be kept in a refrigerator for an extended period of time a composition containing pyruvic acid for topical use is not very stable at an elevated temperature. Therefore, for practical purposes pyruvic acid esters are used instead.

The representative esters are methyl pyruvate, ethyl pyruvate, propyl pyruvate and isopropyl pyruvate. Other representative ketomonocarboxylic acids and their esters are phenyl pyruvic acid and its esters such as methyl phenyl pyruvate, ethyl phenyl pyruvate and propyl phenyl pyruvate; formyl formic acid (2-ketoacetic acid) and its esters such as methyl, ethyl and propyl formyl formate; benzoyl formic acid and its esters such as methyl, ethyl and propyl benzoyl formate; 4-hydroxybenzoylformic acid and its esters; 4-hydroxyphenylpyruvic acid and its esters; 2-hydroxyphenylpyruvic acid and its esters.

Many hydroxy or ketomonocarboxylic acids are structurally related to amino acids either naturally occurring in proteins or not. For example alanine and pyruvic acid are interconverted to each other in vivo by an enzyme alanine dehydrogenase or alanine ketoglutarate transaminase. As mentioned earlier pyruvic acid and lactic acid are interconverted to each other in vivo by the enzyme lactate dehydrogenase. Therefore, alanine, pyruvic acid and lactic acid are chemically related in that the amino group of alanine may be converted to the keto group of pyruvic acid or the hydroxy group of lactic acid. The same relationships may apply to formyl formic acid and glycolic acid to glycine; hydroxypyruvic acid and glyceric acid to serine; phenyl pyruvic acid and phenyl lactic acid to phenylalanine; 2-keto- and 2-hydroxy-4 (methylthio) butanoic acids to methionine.

The second kind of hydroxyacid is hydroxydicarboxylic acid having the following chemical structure:



wherein

$m=1, 2, 3, 4, 5, 6, 7, 8$ or 9

$n=0$ or a numerical number up to 23

The hydroxydicarboxylic acid may also be present as a free acid, lactone or salt form. The lactone form could be either inter or intramolecular lactone. However, the common lactone is an intramolecular lactone with a ring structure formed by elimination of one or more water molecule between a hydroxy group and one of the carboxylic groups. Since the hydroxydicarboxylic acid is organic in nature, it may form a salt or a complex with an inorganic or organic base such

as ammonium hydroxide, sodium or potassium hydroxide, or triethanolamine.

The hydroxydicarboxylic acid and its related compounds may also exist as stereoisomers such as D, L, DL and meso forms.

The hydrogen atom attached to the carbon atom may be substituted by a nonfunctional element such as F, Cl, Br, I, S or a radical such as a lower alkyl or alkoxy of saturated or unsaturated, having 1 to 9 carbon atoms.

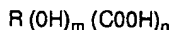
When $n=0$ and $m=1$ or more, the hydroxydicarboxylic acid is also called aldaric acid. The name comes from the carbohydrate, and the common ones are saccharic acid and galactaric acid. Representative hydroxydicarboxylic acids are listed below:

1. 2-Hydroxypropanedioic acid (Tartronic acid)
 $m=1, n=0$
2. 2-Hydroxybutanedioic acid (Malic acid)
 $m=1, n=1$
3. Erythruric acid and Threauric acid (Tartaric acid)
 $m=2, n=0$
4. Araburic acid, Riburic acid, Xyluric acid and Lyxuric acid
 $m=3, n=0$
5. Glucaric acid (saccharic acid), Galactaric acid (Mucic acid), Mannuric acid, Gularic acid, Alluric acid, Altruric acid, Iduric acid and Talaric acid
 $m=4, n=0$

Commercially available saccharolactone (D-saccharic acid 1, 4-lactone) is an intramolecular lactone formed by elimination of one water molecule between the hydroxy group at position 4 and the carboxylic group at position 1.

The third type of hydroxyacid is a miscellaneous group of compounds which is not readily represented by the above generic structure of either the first type or the second type. Included in the third type of hydroxyacids are the following:

Hydroxycarboxylic acid of



Wherein $m, n = 1, 2, 3, 4, 5, 6, 7, 8, \text{ or } 9$

$R=H$, alkyl, aralkyl or aryl group of saturated or unsaturated, straight or branched chain or cyclic form, having 1 to 25 carbon atoms.

citric acid, isocitric acid, citramalic acid, agaricic acid (n-hexadecylcitric acid), quinic acid, uronic acids including glucuronic acid, glucuronolactone, galacturonic acid, galacturonolactone, hydroxypyruvic acid, hydroxypyruvic acid phosphate, ascorbic acid, dihydroascorbic acid, dihydroxytartaric acid, 2-hydroxy-2-methylbutanoic acid, 1-hydroxy-1-cyclopropane carboxylic acid, 2-hydroxyhexanedial, 5-hydroxylysine, 3-hydroxy-2-aminopentanoic acid, tropic acid, 4-hydroxy-2, 2-diphenylbutanoic acid, 3-hydroxy-3-methylglutaric acid, and 4-hydroxy-3-pentenoic acid.

The third type of hydroxyacid may also be present as a free acid, lactone or salt form. The lactone form could be either an inter or intramolecular lactone, however, most common are intramolecular lactones with a ring structure. Commonly known glucuronolactone is a γ -lactone i.e. 1,4-lactone of intramolecular type.

The hydroxyacid of the third type may also exist as stereoisomers such as D, L, DL and meso forms. The hydrogen atom attached to the carbon atom may be substituted by a nonfunctional element such as F, Cl, Br, I, S or a radical such as a lower alkyl or alkoxy of saturated or unsaturated, having 1 to 9 carbon atoms.

In the present invention, the following aspects are disclosed:

A therapeutic composition for use in the treatment of wrinkles comprises an effective amount of at least one compound selected from the group consisting of:

Citramalic acid, Diphenyl 2-hydroxyacetic acid (benzilic acid), 2-phenyl 3-hydroxypropanoic acid (tropic acid), aleuritic acid, ribonic acid, ribonolactone, 2,3,4-trihydroxybutanoic acid, 2,3,4,5-tetrahydroxypentanoic acid, 2,3,4,5,6-pentahydroxyhexanoic acid, 2-hydroxylauric acid, 2,3,4,5,6,7-hexahydroxyheptanoic acid, 4-hydroxymandelic acid, 4-chloromandelic acid, 2-hydroxy-3-methylbutanoic acid, 2-hydroxy-4-methylpentanoic acid, 3-hydroxy-4-methoxymandelic acid, 4-hydroxy-3-methoxymandelic acid, 3-(3-hydroxyphenyl) lactic acid, 3-(4-hydroxyphenyl) lactic acid, hexahydromandelic acid, 3-hydroxy-3-methylpentanoic acid, 1-hydroxy-1-cyclopropane carboxylic acid, 4-hydroxybutanoic acid, 2-hydroxyhexanoic acid, 5-hydroxylauric acid, 12-hydroxylauric acid, 10-hydroxydecanoic acid, 16-hydroxyhexadecanoic acid, 4-hydroxydecanoic acid, 5-hydroxydecanoic acid, and 4-hydroxy-2, 2-diphenylbutanoic acid as a free acid or salt form in a pharmaceutically or cosmetically

acceptable vehicle.

Further, a method for alleviating the symptoms of wrinkles comprising the topical application of a therapeutic effective amount of at least one compound selected from the group consisting of:

Diphenyl 2-hydroxyacetic acid (benzilic acid), 2-phenyl 3-hydroxypropanoic acid (tropic acid), aleuritic acid, ribonic acid, ribonolactone, 2,3,4-trihydroxybutanoic acid, 2,3,4,5-tetrahydroxypentanoic acid, 2,3,4,5,6-pentahydroxyhexanoic acid, 2-hydroxylauric acid, 2,3,4,5,6,7-hexahydroxyheptanoic acid, 4-hydroxymandelic acid, 4-chloromandelic acid, 2-hydroxy-3-methylbutanoic acid, 2-hydroxy-4-methylpentanoic acid, 3-hydroxy-4-methoxymandelic acid, 4-hydroxy-3-methoxymandelic acid, 3-(2-hydroxyphenyl) lactic acid, citramalic acid, 3-(4-hydroxyphenyl) lactic acid, hexahydromandelic acid, 3-hydroxy-3-methylpentanoic acid, 1-hydroxy-1-cyclopropane carboxylic acid, 4-hydroxybutanoic acid, 2-hydroxyhexanoic acid, 5-hydroxylauric acid, 12-hydroxylauric acid, 10-hydroxydecanoic acid, 16-hydroxyhexadecanoic acid, 4-hydroxydecanoic acid, 5-hydroxydecanoic acid, and 4-hydroxy-2, 2-diphenylbutanoic acid as a free acid or salt form in a pharmaceutically or cosmetically acceptable vehicle is disclosed.

In the said composition as described above, said acids and related compounds include glycolic acid, benzoic acid, tropic acid, lactic acid, malic acid, citric acid, isocitric acid, citramalic acid, tartronic acid, tartaric acid, gluconic acid, galactonic acid, alpha hydroxyisobutyric acid, phenyllactic acid, mandelic acid, atrolactic acid, gluconolactone, galactonolactone, ribonic acid, ribonolactone, pantoic acid, pantolactone, pantothenic acid, alpha hydroxybutyric acid, beta hydroxybutyric acid, quinic acid, pyruvic acid, phenyl pyruvic acid, methyl pyruvate, ethyl pyruvate, ascorbic acid, benzoyl formic acid, methyl benzoyl formate, and ethyl benzoyl formate.

Further, a method for preventing as well as treating wrinkles is disclosed comprising the topical application to involved skin of a composition containing a therapeutic effective amount of at least one member selected from the group consisted of hydroxycarboxylic acids and related ketocarboxylic acids, and ester, lactone or salt forms thereof. In the said method, said hydroxycarboxylic acids and related compounds include 2-hydroxyacetic acid; 2-hydroxypropanoic acid; 2-methyl 2-hydroxypropanoic acid; 2-hydroxybutanoic acid; phenyl 2-hydroxyacetic acid; phenyl 2-methyl 2-hydroxyacetic acid; 3-phenyl 2-hydroxyacetic acid; 2,3-dihydroxypropanoic acid; 2,3,4-trihydroxybutanoic acid, 2,3,4,5-tetrahydroxypentanoic acid, 2,3,4,5,6-pentahydroxyhexanoic acid, 2-hydroxydodecanoic acid, 2,3,4,5,6,7-hexahydroxyheptanoic acid, diphenyl 2-hydroxyacetic acid; 4-hydroxymandelic acid; 4-chloromandelic acid; 3-hydroxybutanoic acid; 4-hydroxybutanoic acid; 2-hydroxyhexanoic acid; 5-hydroxydodecanoic acid, 12-hydroxydodecanoic acid, 10-hydroxydecanoic acid, 16-hydroxyhexadecanoic acid, 2-hydroxy-3-methylbutanoic acid; 2-hydroxy-4-methylpentanoic acid; 3-hydroxy-4-methoxymandelic acid; 4-hydroxy-3-methoxymandelic acid; 2-hydroxy-2-methylbutanoic acid; 3-(2-hydroxyphenyl) lactic acid; 3-(4-hydroxyphenyl) lactic acid; hexahydromandelic acid; 3-hydroxy-3-methylpentanoic acid; 4-hydroxydecanoic acid; 5-hydroxydecanoic acid; aleuritic acid; 2-hydroxypropanedioic acid; 2-hydroxybutanedioic acid; erythraric acid; threarric acid; arabiraric acid; ribaric acid; xylaric acid; lyxaric acid; glucaric acid; galactaric acid; mannaric acid; gularic acid; allaric acid; altraric acid; idaric acid; talaric acid; 2-hydroxy-2-methylbutanedioic acid;

Citric acid, isocitric acid, agaricic acid, quinic acid, glucuronic acid, glucuronolactone, galacturonic acid, galacturonolactone, uronic acids, uronolactones, ascorbic acid, dihydroascorbic acid, dihydroxytartaric acid, tropic acid, ribonolactone, gluconolactone, galactonolactone, gulonolactone, mannonolactone, ribonic acid, gluconic acid, citramalic acid;

Pyruvic acid, hydroxypyruvic acid, hydroxypyruvic acid phosphate, methyl pyruvate, ethyl pyruvate, propyl pyruvate, isopropyl pyruvate; phenyl pyruvic acid, methyl phenyl pyruvate, ethyl phenyl pyruvate, propyl phenyl pyruvate; formyl formic acid, methyl formyl formate, ethyl formyl formate, propyl formyl formate, benzoyl formic acid, methyl benzoyl formate, ethyl benzoyl formate, propyl benzoyl formate, 4-hydroxybenzoyl formic acid, 4-hydroxyphenyl pyruvic acid, 2-hydroxyphenyl pyruvic acid.

Further, a prophylactic and therapeutic composition comprising an effective amount of at least one member selected from the group consisted of hydroxycarboxylic acids and related ketocarboxylic acids, and ester, lactone or salt forms thereof in a pharmaceutically acceptable vehicle for topical treatment of skin wrinkles is disclosed.

In the compositions as described above, said hydroxycarboxylic acids and related compounds include 2-hydroxyacetic acid; 2-hydroxypropanoic acid; 2-methyl 2-hydroxypropanoic acid; 2-hydroxybutanoic acid; phenyl 2-hydroxyacetic acid; phenyl 2-methyl 2-hydroxyacetic acid; 3-phenyl 2-hydroxyacetic acid; 2,3-dihydroxypropanoic acid; 2,3,4-trihydroxybutanoic acid, 2,3,4,5-tetrahydroxypentanoic acid, 2,3,4,5,6-pentahydroxyhexanoic acid, 2-hydroxydodecanoic acid, 2,3,4,5,6,7-hexahydroxyheptanoic acid, diphenyl 2-hydroxyacetic acid; 4-hydroxymandelic acid; 4-chloromandelic acid; 3-hydroxybutanoic acid; 4-hydroxybutanoic acid; 2-hydroxyhexanoic acid; 5-hydroxydodecanoic acid, 12-hydroxydodecanoic acid, 10-hydroxydecanoic acid, 16-hydroxyhexadecanoic acid, 2-hydroxy-3-methylbutanoic acid; 2-hydroxy-4-methylpentanoic acid; 3-hydroxy-4-methoxymandelic acid; 4-hydroxy-3-methoxymandelic acid; 2-hydroxy-2-methylbutanoic acid; 3-(2-hydroxyphenyl) lactic acid; 3-(4-hydroxyphenyl) lactic acid; hexahydromandelic acid; 3-hydroxy-3-methylpentanoic acid; 4-hydroxydecanoic acid; 5-hydroxydecanoic acid; aleuritic acid; 2-hydroxypro-

panedioic acid; 2-hydroxybutanedioic acid; erythraric acid; threarric acid; arabiraric acid; ribaric acid; xylaric acid; lyxaric acid; glucaric acid; galactaric acid; mannaric acid; gularic acid; allaric acid; altraric acid; idaric acid; talaric acid; 2-hydroxy-2-methylbutanedioic acid;

Citric acid, isocitric acid, agaricic acid, quinic acid, glucuronic acid, glucuronolactone, galacturonic acid, galacturonolactone, uronic acids, uronolactones, ascorbic acid, dihydroascorbic acid, dihydroxytartaric acid, tropic acid, ribonolactone, gluconolactone, galactonolactone, gulonolactone, mannonolactone, ribonic acid, gluconic acid, citramalic acid;

Pyruvic acid, hydroxypyruvic acid, hydroxypyruvic acid phosphate, their esters; methyl pyruvate, ethyl pyruvate, propyl pyruvate, isopropyl pyruvate; phenyl pyruvic acid, its esters; methyl phenyl pyruvate, ethyl phenyl pyruvate, propyl phenyl pyruvate; formyl formic acid, its esters; methyl formyl formate, ethyl formyl formate, propyl formyl formate; benzoyl formic acid, its esters; methyl benzoyl formate, ethyl benzoyl formate, propyl benzoyl formate; 4-hydroxybenzoyl formic acid, its esters; 4-hydroxyphenyl pyruvic acid, its esters; 2-hydroxyphenyl pyruvic acid and its esters.

Test results and comparative results

Therapeutic compositions packaged in felt pens as described in the following Examples were provided to 14 patients for treatment of age spots, wrinkles, keratoses and other pigmented skin spots. Each participating patient received two felt pens; i.e. with or without the addition of hydroxyacid to the composition containing hydroquinone. The patients were instructed to apply topically one medication on one side of the body such as on the back of the left hand and the other medication on the other side of the body such as on the back of the right hand. Specific instructions were given to the patients that the medications were applied twice daily and discretely only to the skin lesions of age spots, wrinkles, keratoses, melasmas, lentigines or other pigmented skin spots.

Within one to three weeks, improvement of age spots and keratoses was clinically discernible. After one to three months substantial eradication of age spots, wrinkles and keratoses occurred in all the patients tested. Complete eradication of age spots usually occurred within two to four months of topical administration in most cases. Therapeutic compositions containing higher concentrations of hydroxyacids (10 to 20%) and hydroquinone (3 to 5%) were judged to be more efficient in eradicating age spots, wrinkles and keratoses within shorter periods of time. Without the addition of a hydroxyacid to the composition of hydroquinone, eradication of age spots, wrinkles or keratoses did not occur within four months of time.

It was also found that while compositions containing hydroxyacids without hydroquinone were effective for eradication of keratoses and wrinkles, the compositions were not efficient in eradicating pigmented age spots, melasmas or lentigines within 4 months of time. In any case, with the addition of a hydroxyacid to the composition containing hydroquinone, pigmented age spots, melasmas, lentigines and other pigmented skin spots had been substantially eradicated.

Topical applications were carried out either by bilateral or sequential comparison. In bilateral comparison the subject was instructed to apply one preparation on one side of the body and the other one on the other side of the body. In cases where both sides were involved, the subject was instructed to apply two to three times daily one medication on one side of the body for a period of up to several months of time. The medication was discontinued whenever a total remission of the lesions occurred prior to the test period of up to several months.

For face involvement the subject was instructed to apply two to three times daily one medication on one side of the scalp or the face and the other medication on the other side of the scalp or the face for a period of up to 12 weeks of time.

Sequential administrations of medications were carried out whenever the bilateral comparison was difficult. For example in pruritic conditions (comparative), the subject was instructed to apply four times daily or as often as necessary one medication on the pruritic lesions for two days, then switched to the other medication on the same lesions for another two days, thus to compare which medication was more effective in relieving the itching.

Preparation of the Therapeutic Compositions

To prepare a therapeutic composition in solution form at least one of the aforementioned enhancing compounds of hydroxyacids and a cosmetic or pharmaceutical agent are dissolved in a solution which may consist of ethanol, water, propylene glycol, acetone or other pharmaceutically acceptable vehicles. The concentration of hydroxyacids may range from 0.01 to 99 percent by weight of the total composition. The concentration of the cosmetic or pharmaceutical agent ranges from 0.01 to 40 percent by weight of the total composition.

In the preparation of a therapeutic composition in cream or ointment form at least one of hydroxyacids and one of cosmetic or pharmaceutical agents are initially dissolved in a solvent such as water, ethanol, acetone, propylene glycol or polysorbate 80, the solution thus prepared is then mixed in a conventional manner with commonly available cream or ointment base such as hydrophilic ointment or petrolatum. The concentrations of hydroxyacids, cosmetic and pharmaceutical agents may range from 0.01 to 99 percent by weight of the total composition.

Therapeutic compositions of the instant invention may also be formulated in gel, lotion, shampoo, spray, stick or powder. A typical gel composition of the instant invention utilizes at least one of hydroxyacids and one of cosmetic or pharmaceutical agents dissolved in a mixture of ethanol, water and propylene glycol in a volume ratio of 40:40:20, respectively. A gelling agent such as hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose or ammoniated glycyrrhizinate is then added to the mixture with agitation. The preferred concentration of the gelling agent may range from 0.1 to 4 percent by weight of the total composition.

The following are illustrative examples of formulations and compositions according to this invention. Although the examples utilize only selected compounds and formulations, it should be understood that the following examples are illustrative and not limitative. Therefore, any of the aforementioned hydroxyacids, cosmetic and pharmaceutical agents may be substituted according to the teachings of this invention in the following examples.

Example 1

A prophylactic and therapeutic composition in solution form for age spots and for keratoses may be prepared as follows.

Malic acid 1 gram, gluconolactone 19 grams and citric acid 0.5 gram are dissolved in a mixture of ethanol 30 ml, water 42 ml and glycerin 5 ml. Sodium bisulfite 0.5 g and hydroquinone 2 grams are added with stirring until a clear solution is obtained. The hydroxyacids, malic acid, gluconolactone and citric acid have been added a) as antioxidants to help stabilize the hydroquinone in the composition b) to enhance the penetration and the efficacy of hydroquinone c) to normalize the disturbed keratinization in age spot and keratoses.

The composition thus formulated contains 2% hydroquinone, 1% malic acid, 19% gluconolactone, 0.5% citric acid, and has pH 3.3.

Example 2

A therapeutic composition in solution form for age spots and or keratoses may be formulated as follows.

Alpha hydroxyisobutyric acid (Methylactic acid) 20 grams and citric acid 2 grams are dissolved in a mixture of ethanol 49 ml, water 20 ml and propylene glycol 7 ml. Sodium bisulfite 0.5 g and hydroquinone 2 grams are added with stirring until a clear solution is obtained. The composition thus formulated contains 2% hydroquinone, 2% citric acid, 20% methylactic acid, and has pH 3.6.

Example 3

A therapeutic composition containing hydroquinone and lactic acid in solution form for age spots, keratoses, melasmas, lentigines and other pigmented skin spots may be formulated as follows.

Lactic acid 10 ml, hydroquinone 4 grams and sodium metabisulfite 0.6 gram are dissolved in a mixture of ethanol 70 ml, water 10 ml and propylene glycol 6 ml with stirring until a clear solution is obtained. The composition thus formulated contains 4% hydroquinone, 10% lactic acid, and has pH 4.0. The lactic acid has been added to help stabilize and enhance the penetration and the efficacy of hydroquinone, and also to normalize the disturbed keratinization in the skin lesions. The composition thus formulated is packaged in felt pens for controlled delivery to skin lesions.

Example 4

A therapeutic composition containing hydroquinone and glycolic acid in solution form for age spots, keratoses, melasmas, lentigines and other pigmented skin spots may be formulated as follows.

Glycolic acid 8 grams, hydroquinone 5 grams and sodium metabisulfite 0.5 gram are dissolved in a mixture of ethanol 70 ml, water 10 ml and propylene glycol 7 ml with stirring until a clear solution is obtained. The composition thus formulated contains 5% hydroquinone, 8% glycolic acid, and has pH 3.9. The glycolic acid has been added to help stabilize and enhance the penetration and the efficacy of hydroquinone, and also to normalize the disturbed keratinization in the skin lesions. The composition thus prepared is packaged in felt pens for controlled delivery to skin lesions.

Example 5

A therapeutic composition containing hydroquinone and 2-methyl 2-hydroxypropanoic acid in solution form for age spots, keratoses, melasmas, lentigines and other pigmented skin spots may be formulated as follows.

2-Methyl 2-hydroxypropanoic acid 12 grams, hydroquinone 4 grams and sodium bisulfite 0.3 gram are dissolved in a mixture of ethanol 60 ml, water 20 ml and propylene glycol 4 ml with stirring until a clear solution is obtained. The composition thus formulated contains 4% hydroquinone, 12% 2-methyl 2-hydroxypropanoic acid, and has pH 4.0. The composition solution is packaged in felt pens for controlled delivery to skin lesions. The 2-methyl 2-hydroxypropanoic acid

has been added to help stabilize and enhance the penetration and the efficacy of hydroquinone, and also to normalize the disturbed keratinization in the skin lesions.

Example 6

A composition containing hydroquinone alone in solution form for age spots and keratoses studies may be formulated as follows.

Hydroquinone 5 grams and sodium metal bisulfite 0.5 gram are dissolved in a mixture of ethanol 70 ml, water 15 ml and propylene glycol 10 ml with stirring until a clear solution is obtained. The composition thus prepared contains 5% hydroquinone and has pH 6.0. The composition solution is packaged in felt pens for comparative studies; with or without hydroxyacids on age spots and keratoses.

The hydroxyacids and related compounds which may be useful as dermatologic agents for specific conditions and disorders, namely skin wrinkles, include 2-hydroxyacetic acid; 2-hydroxypropanoic acid; 2-methyl 2-hydroxypropanoic acid; 2-hydroxybutanoic acid; phenyl 2-hydroxyacetic acid; phenyl 2-methyl 2-hydroxyacetic acid; 3-phenyl 2-hydroxypropanoic acid; 2,3-dihydroxypropanoic acid; 2,3,4-trihydroxybutanoic acid; 2,3,4,5,6-pentahydroxyhexanoic acid; 2-hydroxydodecanoic acid; 2,3,4,5-tetrahydroxypentanoic acid; 2,3,4,5,6,7-hexahydroxyheptanoic acid; diphenyl 2-hydroxyacetic acid; 4-hydroxymandelic acid; 4-chloromandelic acid; 3-hydroxybutanoic acid; 4-hydroxybutanoic acid; 2-hydroxyhexanoic acid; 5-hydroxydodecanoic acid; 12-hydroxydodecanoic acid; 10-hydroxydecanoic acid; 16-hydroxyhexadecanoic acid; 2-hydroxy-3-methylbutanoic acid; 2-hydroxy-4-methylpentanoic acid; 3-hydroxy-4-methoxymandelic acid; 4-hydroxy-3-methoxymandelic acid; 2-hydroxy-2-methylbutanoic acid; 3-(2-hydroxyphenyl) lactic acid; 3-(4-hydroxyphenyl) lactic acid; hexahydromandelic acid; 3-hydroxy-3-methylpentanoic acid; 4-hydroxydecanoic acid; 5-hydroxydecanoic acid; aleuritic acid.

2-Hydroxypropanedioic acid; 2-hydroxybutanedioic acid; erythruric acid; threauric acid; araburic acid; riburic acid; xyluric acid; lyxuric acid; glucuric acid; galacturic acid; mannuric acid; guluric acid; alluric acid; altruric acid; iduric acid; 2-hydroxy-2-methylbutanedioic acid.

Citric acid, isocitric acid, agaricic acid, quinic acid, glucuronic acid, glucuronolactone, galacturonic acid, galacturonolactone, uronic acids, uronolactones, ascorbic acid, dihydroascorbic acid, dihydroxytartaric acid, tropic acid, ribonolactone, gluconolactone, galactonolactone, gulonolactone, mannonolactone, citramalic acid.

Pyruvic acid, hydroxypyruvic acid, hydroxypyruvic acid phosphate, their esters; methyl pyruvate, ethyl pyruvate, propyl pyruvate, isopropyl pyruvate; phenyl pyruvic acid, its esters; methyl phenyl pyruvate, ethyl phenyl pyruvate, propyl phenyl pyruvate; formyl formic acid; its esters; methyl formyl formate, ethyl formyl formate, propyl formyl formate; benzoyl formic acid, its esters; methyl benzoyl formate, ethyl benzoyl formate and propyl benzoyl formate; 4-hydroxybenzoyl formic acid, its esters; 4-hydroxyphenyl pyruvic acid, its esters; 2-hydroxyphenyl pyruvic acid and its esters.

Claims

1. Use of at least one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation of a topical dermatologic therapeutic composition for use in the treatment of wrinkles.
2. Use of 2-hydroxyacetic acid as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.
3. Use of 2-hydroxypropanoic acid as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.
4. Use of 2-methyl 2-hydroxypropanoic acid as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.
5. Use of citric acid as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.
6. Use of gluconolactone as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.
7. Use of dihydroxytartaric acid as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.
8. Use as claimed in claim 1, wherein the hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and

salt forms thereof, include 2-hydroxybutanoic acid; phenyl 2-hydroxyacetic acid; phenyl 2-methyl 2-hydroxyacetic acid; 3-phenyl 2-hydroxypropanoic acid; 2,3-dihydroxypropanoic acid; 2,3,4-trihydroxybutanoic acid; 2,3,4,5-tetrahydroxypentanoic acid; 2,3,4,5,6-pentahydroxyhexanoic acid; 2-hydroxydodecanoic acid; 2,3,4,5,6,7-hexahydroxyheptanoic acid; diphenyl 2-hydroxyacetic acid; 4-hydroxymandelic acid; 4-chloromandelic acid; 3-hydroxybutanoic acid; 4-hydroxybutanoic acid; 2-hydroxyhexanoic acid; 5-hydroxydodecanoic acid, 12-hydroxydodecanoic acid, 10-hydroxydecanoic acid, 16-hydroxyhexadecanoic acid, 2-hydroxy-3-methylbutanoic acid; 2-hydroxy-4-methylpentanoic acid; 3-hydroxy-4-methoxymandelic acid; 4-hydroxy-3-methoxymandelic acid; 2-hydroxy-2-methylbutanoic acid; 3-(2-hydroxyphenyl) lactic acid; 3-(4-hydroxyphenyl) lactic acid; hexahydromandelic acid; 3-hydroxy-3-methylpentanoic acid; 4-hydroxydecanoic acid;

5-hydroxydecanoic acid; aleuritic acid; 2-hydroxypropanedioic acid; 2-hydroxybutanedioic acid; erythraric acid; threonic acid; arabiraric acid; ribaric acid; xylaric acid; lyxaric acid; glucaric acid; galactaric acid; mannaric acid; gularic acid; allaric acid; altraric acid; idaric acid; talaric acid; 2-hydroxy-2-methylbutanedioic acid;

isocitric acid, agaricic acid, quinic acid, glucuronic acid, glucuronolactone, galacturonic acid, galacturonolactone, uronic acids, uronolactones, ascorbic acid, dihydroascorbic acid, tropic acid, ribonolactone, galactonolactone, gulonolactone, mannonolactone, ribonic acid, gluconic acid; citramalic acid; pyruvic acid, hydroxypyruvic acid, hydroxypyruvic acid phosphate, their esters; methyl pyruvate, ethyl pyruvate, propyl pyruvate, isopropyl pyruvate; phenyl pyruvic acid, its esters; methyl phenyl pyruvate, ethyl phenyl pyruvate, propyl phenyl pyruvate, formyl formic acid, its esters; methyl formyl formate, ethyl formyl formate, propyl formyl formate; benzoyl formic acid, its esters; methyl benzoyl formate, ethyl benzoyl formate, propyl benzoyl formate; 4-hydroxybenzoyl formic acid, its esters; 4-hydroxyphenylpyruvic acid, its esters; 2-hydroxyphenylpyruvic acid and its esters.

9. Use according to any of claims 1 to 8, wherein the at least one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof is used in the composition in an amount of from 10 to 20%.

10. Use according to any of claims 1 to 9, wherein the wrinkles to be treated are human facial wrinkles.

11. Use of quinic acid as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.

12. Use of ribonolactone as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.

13. Use of 2-hydroxybutanedioic acid as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.

14. Use of 2-phenyl-2-hydroxyacetic acid as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.

15. Use of diphenyl 2-hydroxyacetic acid as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.

16. Use of galactonolactone as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.

17. Use of ethyl 2-ketopropanoate as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.

18. Use of tropic acid as one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the preparation according to claim 1.

19. Use of a topical composition containing at least one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof, for the treatment of wrinkles.

20. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof is 2-hydroxyacetic acid.

21. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof is 2-hydroxypropanoic acid.

22. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and keto-carboxylic acids, and ester, lactone, and salt forms thereof is 2-methyl 2-hydroxypropanoic acid.
- 5 23. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and keto-carboxylic acids, and ester, lactone, and salt forms thereof is citric acid.
24. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and keto-carboxylic acids, and ester, lactone, and salt forms thereof is gluconolactone.
- 10 25. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and keto-carboxylic acids, and ester, lactone, and salt forms thereof is dihydroxytartaric acid.
26. Use of the topical composition as claimed in claim 19, wherein the hydroxycarboxylic acids and ketocarboxylic acids and ester, lactone, and salt forms thereof, include 2-hydroxybutanoic acid; phenyl 2-hydroxyacetic acid; phenyl 2-methyl 2-hydroxyacetic acid; 3-phenyl 2-hydroxypropanoic acid; 2,3-dihydroxypropanoic acid; 2,3,4-trihydroxybutanoic acid; 2,3,4,5-tetrahydroxypentanoic acid; 2,3,4,5,6-pentahydroxyhexanoic acid; 2-hydroxydodecanoic acid; 2,3,4,5,6,7-hexahydroxyheptanoic acid; diphenyl 2-hydroxyacetic acid; 4-hydroxymandelic acid; 4-chloromandelic acid; 3-hydroxybutanoic acid; 4-hydroxybutanoic acid; 2-hydroxyhexanoic acid; 5-hydroxydodecanoic acid; 12-hydroxydodecanoic acid; 10-hydroxydecanoic acid; 16-hydroxyhexadecanoic acid; 2-hydroxy-3-methylbutanoic acid; 2-hydroxy-4-methylpentanoic acid; 3-hydroxy-4-methoxymandelic acid; 4-hydroxy-3-methoxymandelic acid; 2-hydroxy-2-methylbutanoic acid; 3-(2-hydroxyphenyl) lactic acid; 3-(4-hydroxyphenyl) lactic acid; hexahydromandelic acid; 3-hydroxy-3-methylpentanoic acid; 4-hydroxydecanoic acid; 5-hydroxydecanoic acid; aleuritic acid; 2-hydroxypropanedioic acid; 2-hydroxybutanedioic acid; erythraric acid; threarric acid; arabaric acid; ribaric acid; xylaric acid; lyxaric acid; glucaric acid; galactaric acid; mannaric acid; gularic acid; allaric acid; altraric acid; idaric acid; talaric acid; 2-hydroxy-2-methylbutanedioic acid; isocitric acid, agaricic acid, quinic acid, glucuronic acid, glucuronolactone, galacturonic acid, galacturonolactone, uronic acids, uronolactones, ascorbic acid, dihydroascorbic acid, tropic acid, ribonolactone, galactonolactone, gulonolactone, mannonolactone, ribonic acid, gluconic acid, citramalic acid; pyruvic acid, hydroxypyruvic acid, hydroxypyruvic acid phosphate, their esters; methyl pyruvate, ethyl pyruvate, propyl pyruvate, isopropyl pyruvate; phenyl pyruvic acid, its esters; methyl phenyl pyruvate, ethyl phenyl pyruvate, propyl phenyl pyruvate, formyl formic acid, its esters; methyl formyl formate, ethyl formyl formate, propyl formyl formate; benzoyl formic acid, its esters; ethyl benzoyl formate, ethyl benzoyl formate, propyl benzoyl formate; 4-hydroxybenzoyl formic acid, its esters; 4-hydroxyphenylpyruvic acid, its esters; 2-hydroxyphenylpyruvic acid and its esters.
- 35 27. Use of the topical composition of any of claims 19 to 26, wherein the at least one member selected from hydroxycarboxylic acids and ketocarboxylic acids, and ester, lactone, and salt forms thereof is used in the composition in an amount of from 10 to 20%.
28. Use of the topical composition as claimed in any of claims 19 to 27 wherein the wrinkles to be treated are human facial wrinkles.
- 40 29. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and keto-carboxylic acids, and ester, lactone, and salt forms thereof is quinic acid.
- 45 30. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and keto-carboxylic acids, and ester, lactone, and salt forms thereof is ribonolactone.
31. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and keto-carboxylic acids, and ester, lactone, and salt forms thereof is 2-hydroxybutanedioic acid.
- 50 32. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and keto-carboxylic acids, and ester, lactone, and salt forms thereof is 2-phenyl 2-hydroxyacetic acid.
33. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and keto-carboxylic acids, and ester, lactone, and salt forms thereof is diphenyl 2-hydroxyacetic acid.
- 55 34. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and keto-carboxylic acids, and ester, lactone, and salt forms thereof is galactonolactone.

35. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and keto-carboxylic acids, and ester, lactone, and salt forms thereof is ethyl 2-ketopropanoate.

36. Use of the topical composition of claim 19, wherein the member selected from hydroxycarboxylic acids and keto-carboxylic acids, and ester, lactone, and salt forms thereof is tropic acid.

Patentsprüche

1. Verwendung mindestens eines unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählten Bestandteils für die Herstellung einer topischen dermatologischen therapeutischen Zusammensetzung zur Verwendung bei der Behandlung von Falten oder Fältchen.

2. Verwendung von 2-Hydroxyessigsäure als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.

3. Verwendung von 2-Hydroxypropansäure als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.

4. Verwendung von 2-Methyl-2-hydroxypropansäure als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.

5. Verwendung von Citronensäure als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.

6. Verwendung von Gluconolacton als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.

7. Verwendung von Dihydroxyweinsäure als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.

8. Verwendung nach Anspruch 1, worin die Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen 2-Hydroxybutansäure; Phenyl-2-hydroxyessigsäure; Phenyl-2-methyl 2-hydroxyessigsäure; 3-Phenyl-2-hydroxypropansäure; 2,3-Dihydroxypropansäure; 2,3,4-Trihydroxybutansäure; 2,3,4,5-Tetrahydroxypentansäure; 2,3,4,5,6-Pentahydroxyhexansäure; 2-Hydroxydodecansäure; 2,3,4,5,6,7-Hexahydroxyheptansäure; Diphenyl-2-hydroxyessigsäure; 4-Hydroxymandelsäure; 4-Chlormandelsäure; 3-Hydroxybutansäure; 4-Hydroxybutansäure; 2-Hydroxyhexansäure, 5-Hydroxydodecansäure, 12-Hydroxydodecansäure, 10-Hydroxydecanolacton, 16-Hydroxyhexadecansäure, 2-Hydroxy-3-methylbutansäure; 2-Hydroxy-4-methylpentansäure; 3-Hydroxy-4-methoxymandelsäure; 4-Hydroxy-3-methoxymandelsäure; 2-Hydroxy-2-methylbutansäure; 3-(2-Hydroxyphenyl)milchsäure; 3-(4-Hydroxyphenyl)milchsäure; Hexahydromandelsäure; 3-Hydroxy-3-methylpentansäure; 4-Hydroxydecanolacton; 5-Hydroxydecanolacton; Aleuritinsäure; 2-Hydroxypropandisäure; Äpfelsäure; Erythrasäure; Threarsäure; Arabirarsäure; Ribarsäure; Xylarsäure; Lyxarsäure; Glucarsäure; Galactarsäure; Mannarsäure; Gularsäure; Allarsäure; Altrarsäure; Idozuckersäure; Talarsäure; 2-Hydroxy-2-methylbernsteinsäure; Isocitronensäure, Agaricinsäure, Chinasäure, Glucuronsäure, Glucuronolacton, Galacturonsäure, Galacturonolacton, Uronsäuren, Uronolactone, Ascorbinsäure, Dihydroascorbinsäure, Tropasäure, Ribonolacton, Galactonolacton, Gulonolacton, Mannonolacton, Ribonsäure, Gluconsäure; Citramalsäure; Brenztraubensäure, Hydroxybrenztraubensäure, Hydroxybrenztraubensäure-phosphat, deren Ester; Brenztraubensäuremethylester, Brenztraubensäureethylester, Brenztraubensäurepropylester, Brenztraubensäureisopropylester; Phenylbrenztraubensäure, deren Ester; Phenylbrenztraubensäuremethylester, Phenylbrenztraubensäureethylester, Phenylbrenztraubensäurepropylester, Formylameisensäure, deren Ester; Formylameisensäuremethylester, Formylameisensäureethylester, Formylameisensäurepropylester; Benzoylameisensäure, deren Ester; Benzoylameisensäuremethylester, Benzoylameisensäureethylester, Benzoylameisensäurepropylester; 4-Hydroxybenzoylameisensäure, deren Ester; 4-Hydroxyphenylbrenztraubensäure, deren Ester; 2-Hydroxyphenylbrenztraubensäure und deren Ester umfassen.

9. Verwendung nach einem der Ansprüche 1 bis 8, worin der mindestens eine unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil in der Zusammensetzung in einer Menge von 10 bis 20 % verwendet wird.

10. Verwendung nach einem der Ansprüche 1 bis 9, worin die zu behandelnden Falten oder Fältchen menschliche Gesichtsfalten oder -fältchen sind.

11. Verwendung von Chinasäure als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.
- 5 12. Verwendung von Ribonlacton als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.
13. Verwendung von Äpfelsäure als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.
- 10 14. Verwendung von 2-Phenyl-2-hydroxyessigsäure als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.
- 15 15. Verwendung von Diphenyl-2-hydroxyessigsäure als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.
- 16 16. Verwendung von Galactonlacton als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.
- 20 17. Verwendung von 2-Ketopropansäureethylester als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.
18. Verwendung von Tropasäure als ein unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählter Bestandteil für die Herstellung nach Anspruch 1.
- 25 19. Verwendung einer topischen Zusammensetzung, die mindestens einen unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählten Bestandteil enthält, für die Behandlung von Falten oder Fältchen.
- 30 20. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil 2-Hydroxyessigsäure ist.
21. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil 2-Hydroxypropansäure ist.
- 35 22. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil 2-Methyl-2-hydroxypropansäure ist.
23. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil Citronensäure ist.
- 40 24. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil Gluconolacton ist.
- 45 25. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil Dihydroxyweinsäure ist.
- 50 26. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin die Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen 2-Hydroxybutansäure; Phenyl-2-hydroxyessigsäure; Phenyl-2-methyl-2-hydroxyessigsäure; 3-Phenyl-2-hydroxypropansäure; 2,3-Dihydroxypropansäure; 2,3,4-Trihydroxybutansäure; 2,3,4,5-Tetrahydroxypentansäure; 2,3,4,5,6-Pentahydroxyhexansäure; 2-Hydroxydodecansäure; 2,3,4,5,6,7-Hexahydroxyheptansäure; Diphenyl-2-hydroxyessigsäure; 4-Hydroxymandelsäure; 4-Chlormandelsäure; 3-Hydroxybutansäure; 4-Hydroxybutansäure; 2-Hydroxyhexansäure, 5-Hydroxydodecansäure, 12-Hydroxydodecansäure, 10-Hydroxydecansäure, 16-Hydroxyhexadecansäure, 2-Hydroxy-3-methylbutansäure; 2-Hydroxy-4-methylpentansäure; 3-Hydroxy-4-methoxymandelsäure; 4-Hydroxy-3-methoxymandelsäure; 2-Hydroxy-2-methylbutansäure; 3-(2-Hydroxyphenyl)milchsäure; 3-(4-Hydroxyphenyl)milchsäure; Hexahydromandelsäure; 3-Hydroxy-3-methylpentansäure; 4-Hydroxydecansäure; 5-Hydroxydecansäure; Aleuritinsäure; 2-Hydroxypropandisäure; Äpfelsäure; Erythrarsäure; Threarsäure; Arabirarsäure; Ribarsäure; Xylarsäure; Lyxarsäure; Glucarsäure; Galactarsäure; Mannarsäure; Gularsäure; Allarsäure; Altrarsäure; Idozuckersäure; Talarsäure; 2-Hydroxy-2-
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methylnbernsteinsäure; Isocitronensäure, Agaricinsäure, Chinasäure, Glucuronsäure, Glucuronlacton, Galacturon-
säure, Galacturonlacton, Uronsäuren, Uronolactone, Ascorbinsäure, Dihydroascorbinsäure, Tropasäure, Ribonlac-
ton, Galactonlacton, Gulonolacton, Mannonolacton, Ribonsäure, Gluconsäure; Citramalsäure; Brenztraubensäure,
Hydroxybrenztraubensäure, Hydroxybrenztraubensäure-phosphat, deren Ester; Brenztraubensäuremethylester,
5 Brenztraubensäureethylester, Brenztraubensäurepropylester, Brenztraubensäureisopropylester; Phenylbrenztrau-
bensäure, deren Ester; Phenylbrenztraubensäuremethylester, Phenylbrenztraubensäureethylester, Phenylbrenz-
traubensäurepropylester, Formylameisensäure, deren Ester; Formylameisensäuremethylester,
Formylameisensäureethylester, Formylameisensäurepropylester; Benzoylameisensäure, deren Ester; Benzoyl-
ameisensäureethylester, Benzoylameisensäureethylester, Benzoylameisensäurepropylester; 4-Hydroxybenzoyl-
10 ameisensäure, deren Ester; 4-Hydroxyphenylbrenztraubensäure, deren Ester; 2-
Hydroxyphenylbrenztraubensäure und deren Ester umfassen.

27. Verwendung der topischen Zusammensetzung nach einem der Ansprüche 19 bis 26, worin der mindestens eine
15 unter Hydroxycarbonsäuren und Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte
Bestandteil in der Zusammensetzung in einer Menge von 10 bis 20 % verwendet wird.

28. Verwendung der topischen Zusammensetzung nach einem der Ansprüche 19 bis 27, worin die zu behandelnden
Falten oder Fältchen menschliche Gesichtsfalten oder -fältchen sind.

29. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und
Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil Chinasäure ist.

30. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und
Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil Ribonolacton ist.

31. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und
Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil Äpfelsäure ist.

32. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und
Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil 2-Phenyl-2-hydroxyessig-
säure ist.

33. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und
Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil Diphenyl-2-hydroxyessig-
säure ist.

34. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und
Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil Galactonolacton ist.

35. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und
Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil 2-Ketopropansäureethyle-
ster ist.

36. Verwendung der topischen Zusammensetzung nach Anspruch 19, worin der unter Hydroxycarbonsäuren und
Ketocarbonsäuren und deren Ester-, Lacton- und Salzformen ausgewählte Bestandteil Tropasäure ist.

Revendications

1. Utilisation d'au moins un élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques,
50 ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation d'une composition dermatologique topi-
que thérapeutique destinée à être utilisée pour le traitement des rides.

2. Utilisation de l'acide 2-hydroxyacétique comme élément choisi parmi les acides hydroxycarboxyliques et les acides
céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendica-
55 tion 1.

3. Utilisation de l'acide 2-hydroxypropanoïque comme élément choisi parmi les acides hydroxycarboxyliques et les
acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la
revendication 1.

4. Utilisation de l'acide 2-méthyl-2-hydroxypropanoïque comme élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendication 1.
5. Utilisation de l'acide citrique comme élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendication 1.
6. Utilisation de la gluconolactone comme élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendication 1.
7. Utilisation de l'acide dihydroxytartrique comme élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendication 1.
8. Utilisation selon la revendication 1, les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que leurs formes esters, lactones et sels, comprenant l'acide 2-hydroxybutanoïque, l'acide phényl-2-hydroxyacétique, l'acide phényl-2-méthyl-2-hydroxyacétique, l'acide 3-phényl-2-hydroxypropanoïque, l'acide 2,3-dihydroxypropanoïque, l'acide 2,3,4-trihydroxybutanoïque, l'acide 2,3,4,5-tétrahydroxypentanoïque, l'acide 2,3,4,5,6-pentahydroxyhexanoïque, l'acide 2-hydroxydodécanoïque, l'acide 2,3,4,5,6,7-hexahydroxyheptanoïque, l'acide diphenyl-2-hydroxyacétique, l'acide 4-hydroxymandélique, l'acide 4-chloromandélique, l'acide 3-hydroxybutanoïque, l'acide 4-hydroxybutanoïque, l'acide 2-hydroxyhexanoïque, l'acide 5-hydroxydodécanoïque, l'acide 12-hydroxydodécanoïque, l'acide 10-hydroxydécanoïque, l'acide 16-hydroxyhexadécanoïque, l'acide 2-hydroxy-3-méthylbutanoïque, l'acide 2-hydroxy-4-méthylpentanoïque, l'acide 3-hydroxy-4-méthoxymandélique, l'acide 4-hydroxy-3-méthoxymandélique, l'acide 2-hydroxy-2-méthylbutanoïque, l'acide 3-(2-hydroxyphényl)lactique, l'acide 3-(4-hydroxyphényl)lactique, l'acide hexahydromandélique, l'acide 3-hydroxy-3-méthylpentanoïque, l'acide 4-hydroxydécanoïque, l'acide 5-hydroxydécanoïque, l'acide aleuritique, l'acide 2-hydroxypropanedioïque, l'acide 2-hydroxybutanedioïque, l'acide érythrrique, l'acide thréarrique, l'acide arabarrique, l'acide ribarrique, l'acide xylarrique, l'acide lyxarrique, l'acide glucarrique, l'acide galactarrique, l'acide mannarrique, l'acide gularrique; l'acide allarrique, l'acide altrarrique, l'acide idarrique, l'acide talarrique, l'acide 2-hydroxy-2-méthylbutanedioïque, l'acide isocitrique, l'acide agaricrique, l'acide quinique, l'acide glucuronique, la glucuronolactone, l'acide galacturonique, la galacturonolactone, les acides uroniques, les uronolactones, l'acide ascorbrique, l'acide dihydroascorbrique, l'acide tropique, la ribonolactone, la galactonolactone, la gulonolactone, la mannonolactone, l'acide ribonique, l'acide gluconique, l'acide citramalique, l'acide pyruvique, l'acide hydroxypyruvique, le phosphate de l'acide hydroxypyruvique, leurs esters, le pyruvate de méthyle, le pyruvate d'éthyle, le pyruvate de propyle, le pyruvate d'isopropyle, l'acide phénylpyruvique et ses esters, le pyruvate de méthylphényle, le pyruvate d'éthylphényle, le pyruvate de propylphényle, l'acide formylformique et ses esters, le formiate de méthylformyle, le formiate d'éthylformyle, le formiate de propylformyle, l'acide benzoylformique et ses esters, le formiate de méthylbenzoyle, le formiate d'éthylbenzoyle, le formiate de propylbenzoyle, l'acide 4-hydroxybenzoyle et ses esters, l'acide 4-hydroxyphénylpyruvique et ses esters, l'acide 2-hydroxyphénylpyruvique et ses esters.
9. Utilisation selon l'une quelconque des revendications 1 à 8, l'élément minimal choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, étant utilisé dans la composition en une quantité de 10 à 20 %.
10. Utilisation selon l'une quelconque des revendications 1 à 9, les rides à traiter étant les rides du visage humain.
11. Utilisation de l'acide quinique comme élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendication 1.
12. Utilisation de la ribonolactone comme élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendication 1.
13. Utilisation de l'acide 2-hydroxybutanedioïque comme élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendication 1.
14. Utilisation de l'acide 2-phényl-2-hydroxyacétique comme élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendication 1.

15. Utilisation de l'acide diphényl-2-hydroxyacétique comme élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendication 1.
- 5 16. Utilisation de la galactonolactone comme élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendication 1.
17. Utilisation du 2-cétopropanoate d'éthyle comme élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendication 1.
- 10 18. Utilisation de l'acide tropique comme élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour la préparation selon la revendication 1.
- 15 19. Utilisation d'une composition topique contenant au moins un élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, pour le traitement des rides.
- 20 20. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est l'acide 2-hydroxyacétique.
- 25 21. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est l'acide hydroxypropanoïque.
- 30 22. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est l'acide 2-méthyl-2-hydroxypropanoïque.
- 35 23. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est l'acide citrique.
- 40 24. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est la gluconolactone.
- 45 25. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est l'acide dihydroxytartrique.
- 50 26. Utilisation de la composition topique selon la revendication 19, dans laquelle les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, comprennent l'acide 2-hydroxybutanoïque, l'acide phényl-2-hydroxyacétique, l'acide phényl-2-méthyl-2-hydroxyacétique, l'acide 3-phényl-2-hydroxypropanoïque, l'acide 2,3-dihydroxypropanoïque, l'acide 2,3,4-trihydroxybutanoïque, l'acide 2,3,4,5-tétra-hydroxypentanoïque, l'acide 2,3,4,5,6-pentahydroxyhexanoïque, l'acide 2-hydroxydodécanoïque, l'acide 2,3,4,5,6,7-hexahydroxyheptanoïque, l'acide diphényl-2-hydroxyacétique, l'acide 4-hydroxymandélique, l'acide 4-chloromandélique, l'acide 3-hydroxybutanoïque, l'acide 4-hydroxybutanoïque, l'acide 2-hydroxyhexanoïque, l'acide 5-hydroxydodécanoïque, l'acide 12-hydroxydodécanoïque, l'acide 10-hydroxydécanoïque, l'acide 16-hydroxyhexadécanoïque, l'acide 2-hydroxy-3-méthylbutanoïque, l'acide 2-hydroxy-4-méthylpentanoïque, l'acide 3-hydroxy-4-méthoxymandélique, l'acide 4-hydroxy-3-méthoxymandélique, l'acide 2-hydroxy-2-méthylbutanoïque, l'acide 3-(2-hydroxyphényl)lactique, l'acide 3-(4-hydroxyphényl)lactique, l'acide hexahydromandélique, l'acide 3-hydroxy-3-méthylpentanoïque, l'acide 4-hydroxydécanoïque, l'acide 5-hydroxydécanoïque, l'acide aleuritique, l'acide 2-hydroxypropanedioïque, l'acide 2-hydroxybutanedioïque, l'acide érythrrique, l'acide thréarrique, l'acide arabirrique, l'acide ribarrique, l'acide xylarrique, l'acide lyxarrique, l'acide glucarrique, l'acide galactarrique, l'acide mannarrique, l'acide gularrique; l'acide allarrique, l'acide altrarrique, l'acide idarrique, l'acide talarrique, l'acide 2-hydroxy-2-méthylbutanedioïque, l'acide isocitrique, l'acide agarrique, l'acide quinique, l'acide glucuronique, la glucuronolactone, l'acide galacturonique, la galacturonolactone, les acides uroniques, les uronolactones, l'acide ascorbique,
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l'acide dihydroascorbique, l'acide tropique, la ribonolactone, la galactonolactone, la gulonolactone, la mannonolactone, l'acide ribonique, l'acide gluconique, l'acide citramalique, l'acide pyruvique, l'acide hydroxypyruvique, le phosphate de l'acide hydroxypyruvique, leurs esters, le pyruvate de méthyle, le pyruvate d'éthyle, le pyruvate de propyle, le pyruvate d'isopropyle, l'acide phénylpyruvique et ses esters, le pyruvate de méthylphényle, le pyruvate d'éthylphényle, le pyruvate de propylphényle, l'acide formylformique et ses esters, le formiate de méthylformyle, le formiate d'éthylformyle, le formiate de propylformyle, l'acide benzoylformique et ses esters, le formiate de méthylbenzoyle, le formiate d'éthylbenzoyle, le formiate de propylbenzoyle, l'acide 4-hydroxybenzoyle et ses esters, l'acide 4-hydroxyphénylpyruvique et ses esters, l'acide 2-hydroxyphénylpyruvique et ses esters.

27. Utilisation de la composition topique selon l'une quelconque des revendications 19 à 26, dans laquelle l'élément minimal choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est utilisé dans la composition en une quantité de 10 à 20 %.
28. Utilisation de la composition topique selon l'une quelconque des revendications 19 à 27, les rides à traiter étant les rides du visage humain.
29. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est l'acide quinique.
30. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est la ribonolactone.
31. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est l'acide 2-hydroxybutanedioïque.
32. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est l'acide 2-phényl-2-hydroxyacétique.
33. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est l'acide diphenyl-2-hydroxyacétique.
34. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est la galactonolactone.
35. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est le 2-cétopropanoate d'éthyle.
36. Utilisation de la composition topique selon la revendication 19, dans laquelle l'élément choisi parmi les acides hydroxycarboxyliques et les acides céto-carboxyliques, ainsi que les formes esters, lactones et sels de ceux-ci, est l'acide tropique.